

IN THE CLAIMS

1. (currently amended) A single chain T cell receptor (scTCR) comprising:

an α segment constituted by a TCR α chain variable region sequence fused to the N terminus of a TCR α chain constant region extracellular sequence,

a β segment constituted by a TCR β chain variable region sequence fused to the N terminus of a TCR β chain constant region extracellular sequence, and

a linker sequence linking the C terminus of the α segment to the N terminus of the β segment, or vice versa,

the constant region extracellular sequences of the α and β segments being linked by a disulfide bond,

the length of the linker sequence and the position of the disulfide bond being such that the variable region sequences of the α and β segments are mutually orientated substantially as in native $\alpha\beta$ T cell receptors, wherein the scTCR is selected from the group consisting of:

(a) an scTCR wherein the constant region extracellular sequence of the α segment includes a sequence corresponding to TRAC*01 and the β segment includes a sequence corresponding to TRBC1*01 or TRBC2*01, and the said non-native disulfide bond is between cysteine residues substituted for Thr 48 of exon 1 of TRAC*01 and Ser 57 of exon 1 of TRBC1 *01 or TRBC2*01;

(b) an scTCR wherein a disulfide bond links cysteine residues substituted for Thr 45 of exon 1 of TRAC*01 and Ser 77 of exon 1 of TRBC1*01 or TRBC2*01;

(c) an scTCR wherein a disulfide bond links cysteine residues substituted for Tyr 10 of exon 1 of TRAC*01 and Ser 17 of exon 1 of TRBC1*01 or TRBC2*01;

(d) an scTCR wherein a disulfide bond links cysteine residues substituted for Thr 45 of exon 1 of TRAC*01 and Asp 59 of exon 1 of TRBC1*01 or TRBC2*01; and

(e) an scTCR wherein a disulfide bond links cysteine residues substituted for Ser 15 of exon 1 of TRAC*01 and Glu 15 of exon 1 of TRBC1*01 or TRBC2*01.

2-4. (canceled)

5. (previously presented) A scTCR as claimed in claim 3 wherein the constant region extracellular sequence present in the α segment includes a sequence corresponding to the extracellular constant Ig domain of a TCR α chain, and/or the constant region extracellular sequence present in the β segments includes a sequence corresponding to the extracellular constant Ig domain of a TCR β chain.

6. (previously presented) A scTCR as claimed in claim 1 wherein (a) the α segment is the variable region of a TCR fused to the N terminus of the extracellular domain of the α chain constant region of a TCR α chain; and/or (b) the β segment is the variable region of a TCR β chain fused to the N terminus of the extracellular domain of the constant region of a TCR β chain.

7. (previously presented) A scTCR as claimed in claim 1 wherein the constant region extracellular sequences present in the α and β segments correspond to the constant regions of the

α and β chains of a native TCR truncated at their C termini such that the cysteine residues which form the native interchain disulfide bond of the TCR are excluded.

8. (previously presented) A scTCR as claimed in claim 1 wherein the constant region extracellular sequences present in the α and β segments correspond to the constant regions of the α and β chains of a native TCR in which cysteine residues which form the native interchain disulfide bond are substituted by another amino acid residue.

9. (original) A scTCR as claimed in claim 8, wherein the said cysteine residues are substituted by serine or alanine.

10. (previously presented) A scTCR as claimed in claim 1 wherein the linker sequence has the formula -P-AA-P- wherein P is proline and AA represents an amino acid sequence wherein the amino acids are glycine and serine.

11. (previously presented) A scTCR as claimed in claim 1 wherein the linker sequence links the C terminus of the α domain to the N terminus of the β domain.

12. (original) A scTCR as claimed in claim 11 wherein the linker sequence consists of from 26 to 41 amino acids.

13. (original) A scTCR as claimed in claim 11 wherein the linker sequence consists of 29, 30, 31 or 32 amino acids.

14. (original) A scTCR as claimed in claim 11 wherein the linker sequence consists of 33, 34, 35 or 36 amino acids.

15. (currently amended) A scTCR as claimed in claim 11 wherein the linker sequence is- PGGG-(SGGGG)₅-P- (SEQ ID NO:1) wherein P is proline, G is glycine and S is serine.

16. (currently amended) A scTCR as claimed in claim 11 wherein the linker sequence is- PGGG-(SGGGG)₆-P- (SEQ ID NO:34) wherein P is proline, G is glycine and S is serine.

17. (previously presented) A sTCR as claimed in claim 1 in which an unpaired cysteine residue present in native TCR β chain is not present.

18. (previously presented) A scTCR as claimed in claim 1, wherein the constant region extracellular sequence of the α segment includes a sequence corresponding to TRAC*01 and the β segment includes a sequence corresponding to TRBC1*01 or TRBC2*01, and the said non-native disulfide bond is between cysteine residues substituted for Thr 48 of exon 1 of TRAC*01 and Ser 57 of exon 1 of TRBC1 *01 or TRBC2*01.

19. (previously presented) A scTCR as claimed in claim 1, wherein a disulfide bond links cysteine residues substituted for Thr 45 of exon 1 of TRAC*01 and Ser 77 of exon 1 of TRBC1*01 or TRBC2*01.

20. (previously presented) A scTCR as claimed in claim 1, wherein a disulfide bond links cysteine residues substituted for Tyr 10 of exon 1 of TRAC*01 and Ser 17 of exon 1 of TRBC1*01 or TRBC2*01.

21. (previously presented) A scTCR as claimed in claim 1, wherein a disulfide bond links cysteine residues substituted for Thr 45 of exon 1 of TRAC*01 and Asp 59 of exon 1 of TRBC1*01 or TRBC2*01.

22. (previously presented) A scTCR as claimed in claim 1, wherein a disulfide bond links cysteine residues substituted for Ser 15 of exon 1 of TRAC*01 and Glu 15 of exon 1 of TRBC1*01 or TRBC2*01.

23. (previously presented) A scTCR as claimed in claim 1, wherein the TCR α and β chain variable region sequences present in the α and β segments together correspond to the functional variable domain of a first TCR, and the TCR α and β chain constant region

extracellular sequences present in the α and β segments correspond to those of a second TCR, the first and second TCRs being from the same species.

24. (previously presented) A scTCR as claimed in claim 1, wherein the TCR α and β chain variable region sequences present in the α and β segments together correspond to the functional variable domain of a first TCR, and the TCR α and β chain constant region extracellular sequences present in the α and β segments correspond to those of a second TCR, the first and second TCRs being from different species.

25. (original) A scTCR as claimed in claim 24 wherein the TCRA and P chain variable region sequences present in the α and β segments together correspond to the functional variable domain of a human TCR, and the TCR and P chain constant region extracellular sequences present in the α and β segments correspond to those of a mouse TCR.

26. (previously presented) A scTCR as claimed in claim 1 wherein the TCR is one which binds a peptide MHC complex.

27. (original) A scTCR as claimed in claim 25 wherein the TCR is one which binds a CD1- antigen complex.

28. (previously presented) A scTCR as claimed in claim 1 wherein the TCR is one which binds a superantigen or a peptide-MHC/superantigen complex.

29. (previously presented) A multivalent T cell receptor (TCR) complex comprising a plurality of sTCRs as claimed in claim 1.

30. (previously presented) A scTCR as claimed in claim 1 which is covalently linked to a therapeutic agent.

31. (previously presented) A scTCR as claimed in claim 1, or a plurality thereof, when attached to a particle or bead.

32. (previously presented) A composition comprising a scTCR as claimed in claim 1 and a pharmaceutically acceptable carrier.

33. (previously presented) A method for detecting a TCR ligand selected from MHC-peptide complexes, CD 1-antigen complexes, superantigens and MHC-peptide/superantigen complexes which comprises: providing a scTCR as claimed in claim 1, or a plurality thereof; contacting the scTCR with the TCR ligand; and detecting binding of the scTCR to the ligand.

34. (previously presented) A method of identifying an inhibitor of the interaction between an scTCR as claimed in claim 1, or a plurality thereof, and a TCR ligand selected from MHC-peptide complexes, CD 1-antigen complexes, superantigens and MHC-peptide/superantigen complexes comprising contacting the scTCR with a scTCR ligand binding partner, in the presence of and in the absence of a test compound, and determining whether the presence of the test compound reduces binding of the scTCR to the TCR ligand, such reduction being taken as identifying an inhibitor.

35. (previously presented) A method of identifying a potential inhibitor of the interaction between an scTCR as claimed in claim 1, or a plurality thereof, and a TCR ligand selected from MHC-peptide complexes, CD 1-antigen complexes, superantigens and MHC-peptide/superantigen complexes comprising contacting the scTCR or scTCR ligand binding partner with a test compound and determining whether the test compound binds to the scTCR and/or the TCR ligand, such binding being taken as identifying a potential inhibitor.

36. (previously presented) A nucleic acid molecule comprising a sequence encoding a scTCR as claimed in claim 1, or a sequence complementary thereto.

37. (original) A vector comprising a nucleic acid molecule as claimed in claim 36.